

**Applicant:** Lehmann et al.  
**Application No.:** Not Yet Known

(20) and in that on the lower ends of the dispenser channels of the pipetting automat, respectively, the separating element (7) is provided.

25. (Amended) A device in accordance with Claim 1, characterized in that the separating element (7) on its end distal to the bottom, possesses a fitting for connecting to, or plugging into, a dispenser channel (22), preferably a pipetting automat.

#### REMARKS

Claims 1-25 are currently pending in this application. By this Preliminary Amendment, Applicants have removed the multiple dependencies from the claims as provided by the replacement pages annexed to the International Preliminary Examination Report. A marked-up version of the claims showing these amendments is also attached. Applicants have also submitted a Substitute Specification which incorporates these changes as well as replacement pages 1-3 and 3a from the Article 34 Amendment referenced in the Declaration, which were also attached to the International Preliminary Examination Report. The required headings for the U.S. have also been added. No new matter has been introduced into the application by this amendment or the Substitute Specification.

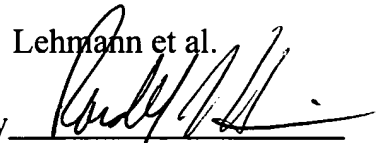
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Prompt examination of the present application is respectfully requested.

Respectfully submitted,

Lehmann et al.

By



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**MARKED-UP VERSION OF THE CLAIMS UNDER 37 CFR §1.121**

3. (Amended) A device in accordance with [Claims 1 or 2] Claim 1, characterized in that one sensor, or a multiplicity of sensors (6), is/are placed on, or in, the bottom of the receptacle (3a) and in that culture areas separated from one another, are formed especially by means of the application of structured, cell repellent coatings or created by means of a three dimensional contouring of the said bottom with recesses or elevations about the separated areas therebetween, and in that the culture medium (4) in the culture areas advantageously is respectively present as drops (25).

4. (Amended) A device in accordance with [one of the Claims 1 to 3] Claim 1, characterized in that the bottom of the receptacle is formed by at least one part of at least one of the wafers which possess the sensor(s) (6).

5. (Amended) A device in accordance with [the generic concept of] Claim 1, characterized in that an open top container, is provided as a receptacle (3), into which a separating element (7) extends, which divides the space of the entire receptacle (3) into two space portions, one positioned above the other, and in that the bottom side space portion forms a small volume reaction space (8) in comparison to the entire volume of the receptacle

(3) and the other space portion forms a reservoir (14) and in that at least one flow channel (9) is provided, which first, communicates with the reaction space (8) and second, communicates with the reservoir space (14) and in that within the separating element (7) one or more through-flow channels (15) are provided, which open into the small volume reaction space (8) of the receptacle (3) and/or in the reservoir space (14) of the receptacle (3).

6. (Amended) A device in accordance with [one of the Claims 1 to 5] Claim 1, characterized in that one or more sensors (6) and/or measurement apparatuses are placed in the area of the reaction space (8, 8a).

7. (Amended) A device in accordance with Claim 5 [or 6], characterized in that the separating element (7) within the receptacle (3) is movable, back and forth, between a position proximal to the bottom and a position remote from the bottom and in the position proximal to the bottom borders the reaction space (8).

8. (Amended) A device in accordance with [one of the Claims 1 to 7] Claim 1, characterized in that the side of the separating element (7) proximal to the bottom, possesses a cover, that is, a bordering surface, for the measurement of the substances

consumed or produced by the cells, especially a surface corresponding to the sensor surface.

9. (Amended) A device in accordance with [one of the Claims 5 to 8] Claim 5, characterized in that the separating element (7) can be inserted from above into the receptacle (3).

10. (Amended) A device in accordance with [one of the Claims 1 to 9] Claim 1, characterized in that the distance of the separating element (7) from the cell culture (2) and therewith the bottom proximal position of the said separating element (7) is adjustable.

11. (Amended) A device in accordance with [one of the Claims 5 to 10] Claim 1, characterized in that the separating element (7) is advantageously constructed in the shape of a hand stamp and has a head (10) with approximately the same cross-section as that of the receptacle (3), and which separating element (7) divides the said receptacle into a reaction space (8) and a reservoir (14) and in that on the separating element (7) a shaft (11) is connected which extends to the outside, the outside cross-section of which shaft (11) is smaller than the open inside cross-section of the receptacle (3) and in that the intervening space between the shaft and the inner wall of the receptacle (3) forms the reservoir (14).

12. (Amended) A device in accordance with [one of the Claims 5 to 11] Claim 5, characterized in that within the separating element (7) one or more flow channels are provided which first, open in the reaction space (8) and second open in the reservoir space (14).

13. (Amended) A device in accordance with [one of the Claims 5 to 12] Claim 5, characterized in that the flow channel (9) is formed by an annular gap provided between the separating element (7) and the inner wall of the receptacle (3) or is designed as a rim profiling, and in that this flow channel, or flow channels remain(s) available, in the case of a separating element (7) which can be adjusted as to height, at least within the lift interval between a position proximal to the bottom and a position remote therefrom.

14. (Amended) A device in accordance with [one of the Claims 1 to 13] Claim 1, characterized in that the underside of the separating element (7) possesses a contouring for the guidance of gas bubbles to the outside, this being preferably a convex bulging.

15. (Amended) A device in accordance with [one of the Claims 5 to 14] Claim 5, characterized in that a thrust limitation for the separating element (7) is provided and in

that for this purpose, in the bottom proximal position an effective restraint is placed on the separating element (7), preferably this being a detent abutted by the upper rim (12) of the receptacle (3).

17. (Amended) A device in accordance with [one of the Claims 1 to 16] Claim 1, characterized in that the separating element (7) possesses on its upper side, an especially standard opening, preferably of a receiving conical shape for the coupling with a pipette, a pipette tip, or a dispenser channel.

18. (Amended) A device in accordance with [one of the Claims 5 to 17] Claim 5, characterized in that the receiving volume of the reservoir (14, 14a) is multiply greater than the receiving volume of the reaction space (8, 8a) and that these two volumes are in relation to one another by the ratios of respectively, 10 : 1 to approximately 100 : 1.

19. (Amended) A device in accordance with [one of the Claims 1 to 18] Claim 1, characterized in that at least on the bottom of the receptacle (3) or a receiver, is placed at least one chip with one or preferably several microsensors.

20. (Amended) A device in accordance with [one of the Claims 1 to 19] Claim 1, characterized in that on the separating element (7), proximal to the reaction space (8) and/or to the reservoir (14), sensors (6) and/or electrodes are provided.

21. (Amended) A device in accordance with [one of the Claims 5 to 20] Claim 5, characterized in that at a distance from the receptacle bottom and between this and the separating element (7) in its bottom proximal position, a microporous membrane (23) or a similar filter or protective covering for the cell culture is provided.

22. (Amended) A device in accordance with [one of the Claims 1 to 21] Claim 1, characterized in that the separating element (7) is comprised of a smooth, cell rejecting, inert and easily sterilized material, this being preferably polytetrafluor ethylene.

23. (Amended) A device in accordance with [one of the Claims 1 to 22] Claim 1, characterized in that the resting surface for the cell culture (2) is optically transparent and in that the resting surface is related to an optical measuring apparatus, which, preferably, is situated on the underside.



24. (Amended) A device in accordance with [one of the Claims 1 to 23] Claim 1, characterized in that a plurality of receptacles (3) are provided, preferably as a part of a pipetting automat (19) and in that these receptacles (3) are especially made by commercially available multiwell plates (20) and in that on the lower ends of the dispenser channels of the pipetting automat, respectively, the separating element (7) is provided.

25. (Amended) A device in accordance with [one of the Claims 1 to 24] Claim 1, characterized in that the separating element (7) on its end distal to the bottom, possesses a fitting for connecting to, or plugging into, a dispenser channel (22), preferably a pipetting automat.